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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHIN, DANA H	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,355	SU ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30,33-35,37-40 and 42* is/are pending in the application.

4a) Of the above claim(s) *1-26,30,35,40 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29,32-34 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on March 5, 2007.

Currently, claims 1-30, 33-35, 37-40, and 42 are pending. Applicants have cancelled claims 31, 36, and 41. Claims 1-26, 30, 35, 40, and 42 have been withdrawn from further consideration as being drawn to a nonelected invention.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

Claims 27-29 and 32-34 remain rejected under 35 U.S.C. 102(e) as being anticipated by Morrissey et al. (US 2003/0206887 A1) for the reasons of record as set forth in the Office action mailed on November 9, 2006 and for the reasons stated below.

The declaration filed on March 5, 2007 under 37 CFR 1.131 has been considered but is ineffective to overcome the Morrissey et al. reference. The evidence submitted is insufficient to

establish a conception of the invention prior to the effective date of the Morrissey et al. reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). Further, the evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Morrissey et al. reference to either a constructive reduction to practice or an actual reduction to practice for the reasons stated below:

Although copies of laboratory notebook pages showing the construct of RNAi-HBVsAg and nucleic acid sequences comprising SEQ ID NO:3 have been provided, there is no evidence that the inventors conceived of the claimed invention and reduced to practice prior to the filing date of Morrissey et al. That is, the showing (Exhibit C) of construction of a vector comprising SEQ ID NO:3 is not sufficient to establish that the inventors conceived of the claimed method of reducing viral expression, viral replication, and viral infection in cells *in vitro* and *in vivo*. Moreover, what is shown in Exhibits A and B is the evidence that the oligonucleotide synthesis for the presently claimed SEQ ID NO:3 had occurred prior to the reference date. This showing of oligonucleotide synthesis does not correlate with applicant's allegation that applicant had conceived of the present invention prior to the effective date of the reference because the instantly claimed invention is directed to methods of reducing the expression of a viral gene in a cell *in vitro* and *in vivo*. In other words, none of the Exhibits submitted under 37 CFR 1.131 sufficiently supports the presently claimed invention, which is more than a mere construction of a vector comprising SEQ ID NO:3. Further, there is no clear indication that the inventors conceived of reducing and inhibiting viral expression with the vector comprising SEQ ID NO:3, because the Exhibits only show oligonucleotide synthesis and construction of an expression

vector comprising the synthesized oligonucleotides. That is, the Exhibits do not show any *in vitro* or *in vivo* methods comprising a vector comprising SEQ ID NO:3, which reduces viral expression or replication in cells as claimed in the instant case. Again, the instantly claimed invention is not directed to a vector comprising SEQ ID NO:3 but to a method of reducing and inhibiting viral expression and replication in a cell *in vitro* and *in vivo*. Taken together, the showing of Exhibits A-C fails to satisfactorily establish reduction to practice or conception of the instantly claimed method for reducing and inhibiting viral expression in a cell with the vector comprising SEQ ID NO:3 prior to the effective date of the reference.

Applicant's arguments filed on March 5, 2007 have been fully considered but they are not persuasive. Applicant argues that Morrissey et al. provide a very broad and general disclosure without enough specific guidance or data and that the disclosure of Morrissey et al. requires guessing, testing, speculation, or 'picking and choosing' to arrive at applicant's claimed method. Contrary to applicant's assertion that the disclosure of Morrissey et al. is broad and general, Morrissey et al. disclosed specific nucleic acid sequences that are potential target sites for hepatitis B virus by identifying them with respective SEQ ID NOs. Further, the instant claims are directed to methods of reducing viral expression and viral replication in a cell. As such, the claims embrace methods performed *in vitro*. Since Morrissey et al. disclose several SEQ ID NOs that specifically embrace instant SEQ ID NO:3 and expressly teach that any one of the disclosed SEQ ID NOs can be used to inhibit HBV expression and replication in a cell (paragraphs 0044, 0046-0047, 0053, 0118, 0275-0276), and since the art of making and using siRNAs *in vitro* did not require undue experimentation at the time the invention of Morrissey et al. was made, the

disclosure of Morrissey et al. would not have required guessing, testing, speculation, or 'picking and choosing' of any skilled artisan to arrive at applicant's method performed *in vitro*.

Further, applicant has not met his burden to prove that any of the disclosed SEQ ID NOs of Morrissey et al. is incapable of inhibiting HBV expression in cells *in vitro*, thereby requiring picking and choosing of a skilled artisan, when the disclosure of Morrissey et al. expressly teaches that any one of the disclosed SEQ ID NOs can be used to inhibit HBV expression and replication in a cell (paragraphs 0044, 0046-0047, 0053, 0118, 0275-0276). More specifically, applicant has not met his burden to prove that a skilled artisan would have guessed, tested, and speculated to pick and choose SEQ ID NOs:66, 712, 1301, and 1378 of Morrissey et al., all of which comprise instant SEQ ID NO:3 and fragments thereof. The fact that Morrissey et al. disclosed four distinct SEQ ID NOs that embrace instantly claimed SEQ ID NO:3 strongly suggests that the target region encompassed by SEQ ID NOs:66, 712, 1301, and 1378 is a preferred region for inhibiting HBV expression in cells.

Further, the Court decision cited in *Air Products and Chemicals, Inc. v. Chas. S. Tanner Co. et al.*, on which applicant bases his argument, is not analogous to the instant case because the prior art references in *Air Products* were found to disclose only some of the claim limitations (e.g., "The Chapman patent does not describe an emulsion polymerization. It describes solution polymerizations which result in products entirely different from the products here at issue", "The Jaffe article itself, however, is silent on the remainder of the composition's makeup", "Roedel does not suggest the use of a protective colloid". See 237-238), and therefore, the Court concluded that the products disclosed in the prior art references did not anticipate the products at issue. Contrary to the *Air Products* case, the Morrissey et al. reference in the instant case teaches

all the claim limitations with specific disclosure of the instantly claimed HBV target sequence for siRNA-mediated gene silencing.

In light of the above, the instantly claimed invention is clearly anticipated by Morrissey et al.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-29, 32-34, and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendments entered in the claims.

Claims 28-29, 33-34, and 38-39 depend from amended claims, therefore the amendments are incorporated in claims 28-29, 33-34, and 38-39.

Claims 27, 32, and 37 are currently amended to recite "the RNA comprises a first nucleotide sequence that hybridizes under stringent conditions to a segment of the gene, and a second nucleotide sequence that is complementary to the first nucleotide sequence and hybridizes to the first nucleotide sequence to form a duplex structure".

The instant specification discloses that "the first nucleotide sequenced is at least 19, e.g., 19-29, nucleotides in length. To inhibit the expression of HBsAg, the first nucleotide sequence is designed to hybridize under stringent conditions to a segment containing one of SEQ ID NOs:1-

10. In one embodiment, the first nucleotide sequence is the same as or complementary to one of these sequences, e.g., SEQ ID NO:3." See pages 1-2. This is the one and only occurrence in which the claimed "first nucleotide" is described throughout the entire specification. As broadly claimed, the metes and bounds encompassed by the term "first nucleotide" is unclear. For example, if the recited first nucleotide comprises 29 nucleotides in length as taught by the specification, one of ordinary skill in the art would not be able to ascertain the remaining composition/nature of the nucleic acids excluding the target segment sequence (e.g., SEQ ID NO:3, which is only 19 nucleotides in length). Since the structure of the claimed RNA comprising first and second nucleotide sequences is unclear, claims 27-29, 32-34, and 37-39 are indefinite.

Conclusion

No claim is allowed.

This application contains claims 1-26, 30, 35, 40, and 42 drawn to an invention nonelected without traverse in the reply filed on October 19, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. Schultz/
J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER